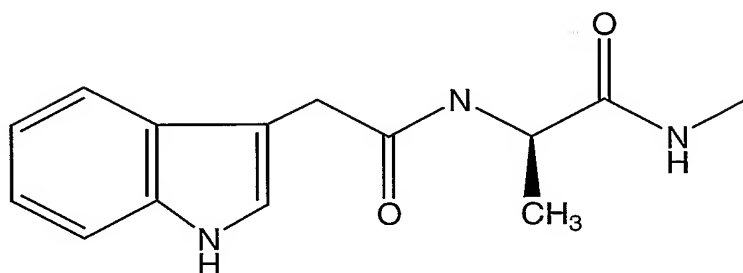
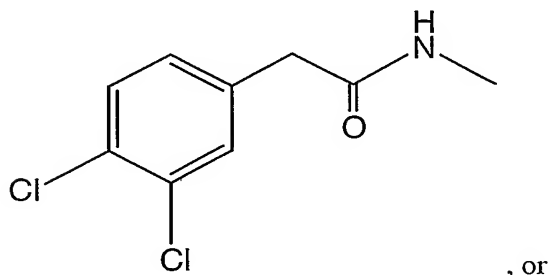


What is claimed is:

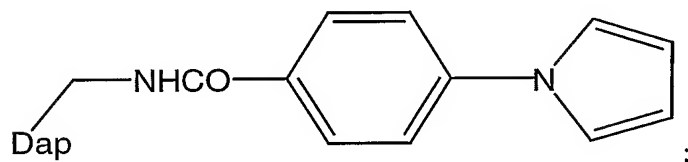
1. An inhibitor of a protein kinase C α (PKC α), the inhibitor comprising A-Ala-Arg-Arg-X-B-Hyd-C-D-, where A =AcHN-,

5

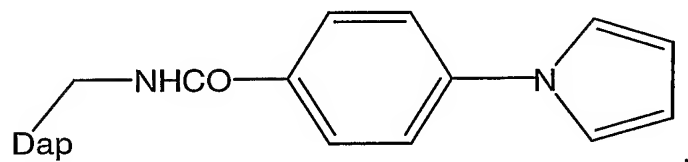


X=any amino acid or amino acid mimetic; B=Ala or a diaminopropionic acid (Dap) derivative having the formula

10



Hyd=Phe, Leu or Ile; C=Arg or Lys; and D=Ala or a Dap derivative having the formula



wherein any of the amino acids can alternatively be an analogous amino acid mimetic.

15

2. The inhibitor of claim 1, having an $IC_{50} < 50 \mu M$ for the PKC α .

3. The inhibitor of claim 1, having an $IC_{50} < 10 \mu M$ for the PKC α .

20

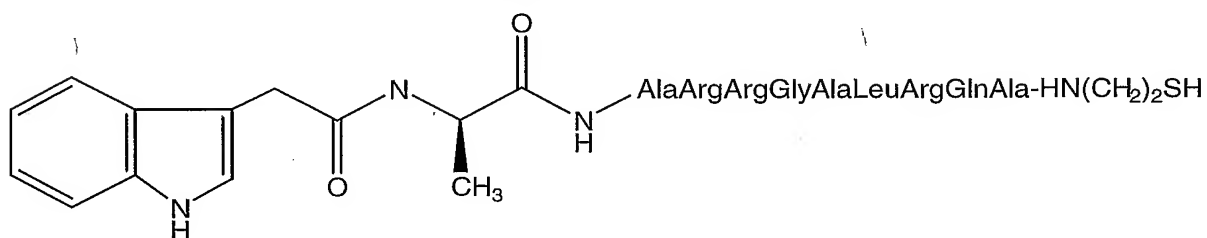
4. The inhibitor of claim 1, having an $IC_{50} < 1 \mu M$ for the PKC α .

5. The inhibitor of claim 1, wherein the inhibitor has an IC_{50} for the PKC α <0.1 that of any other PKC isoform.

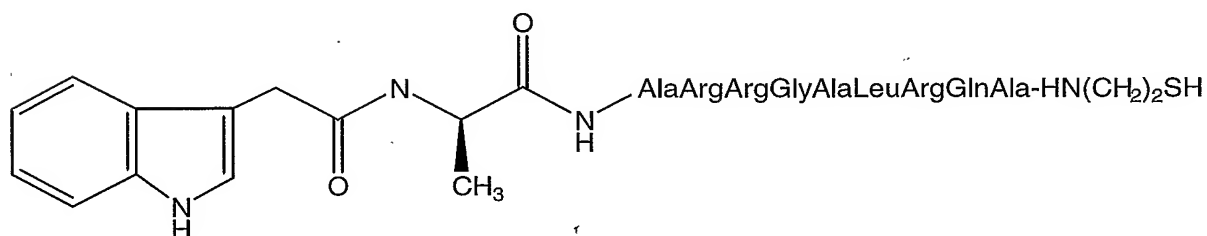
5 6. The inhibitor of claim 1, wherein the inhibitor has an IC_{50} for the PKC α <0.01 that of any other PKC isoform.

7. The inhibitor of claim 1, wherein the PKC α is a human PKC α .

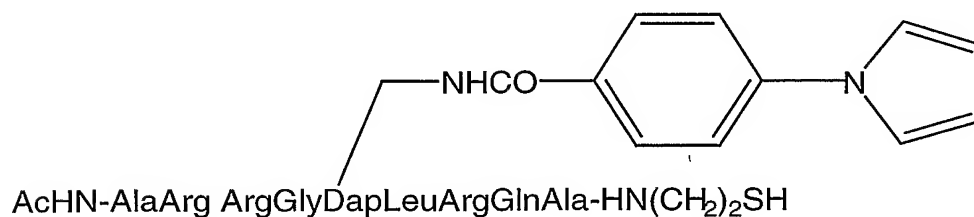
10 8. The inhibitor of claim 1, comprising



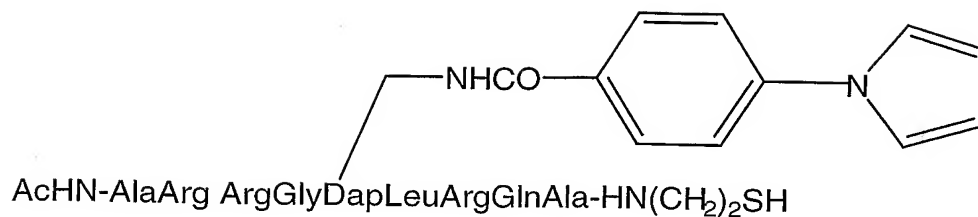
9. The inhibitor of claim 1, consisting of



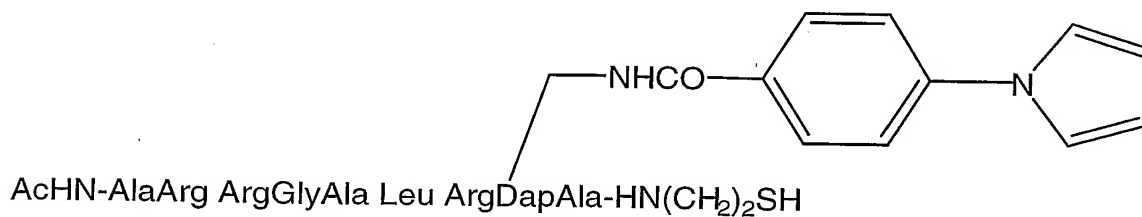
10. The inhibitor of claim 1, comprising



20 11. The inhibitor of claim 1, consisting of

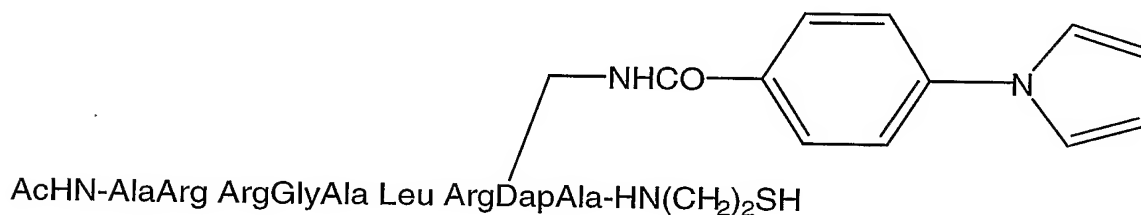


12. The inhibitor of claim 1, comprising

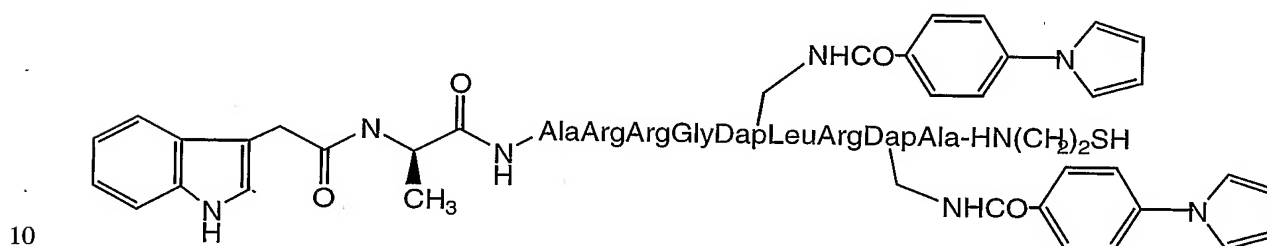


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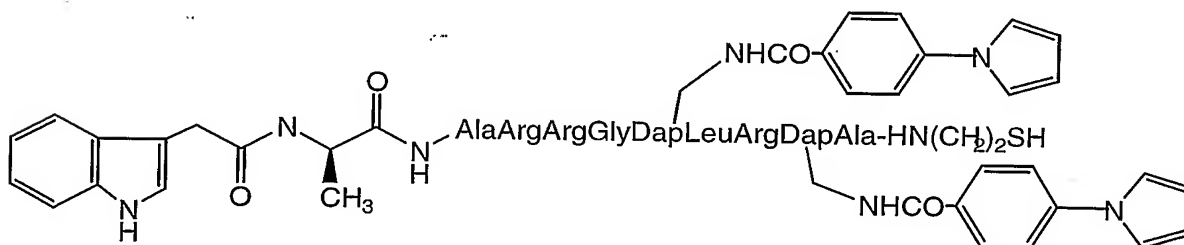
13. The inhibitor of claim 1, consisting of



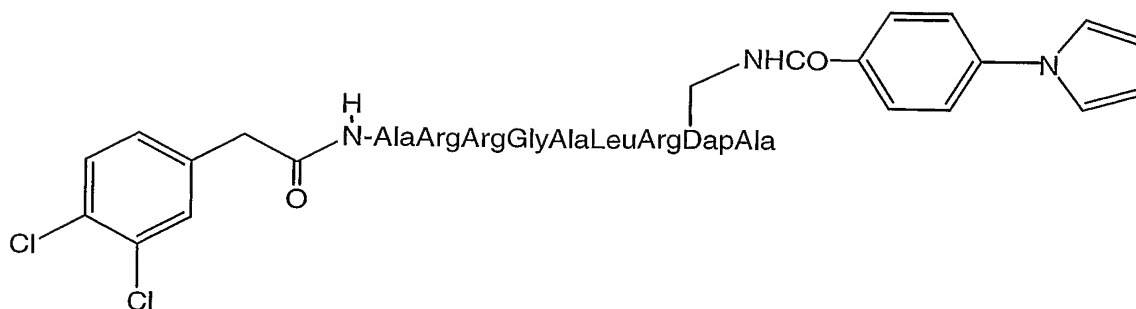
14. The inhibitor of claim 1, comprising



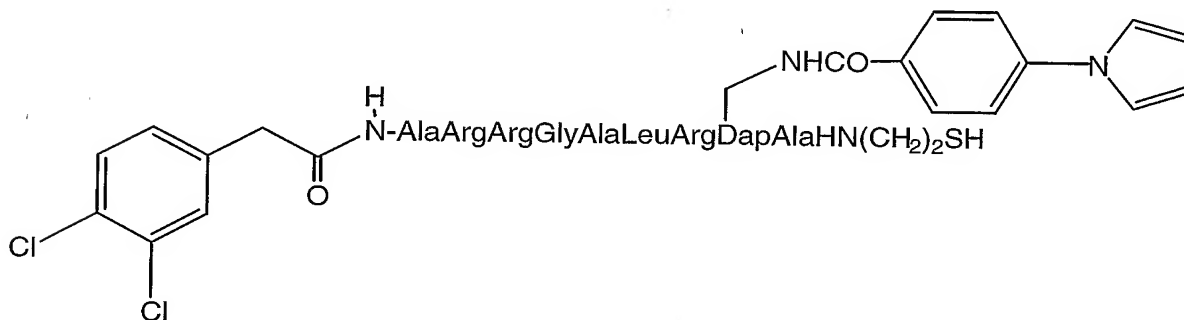
15. The inhibitor of claim 1, consisting of



16. The inhibitor of claim 1, comprising

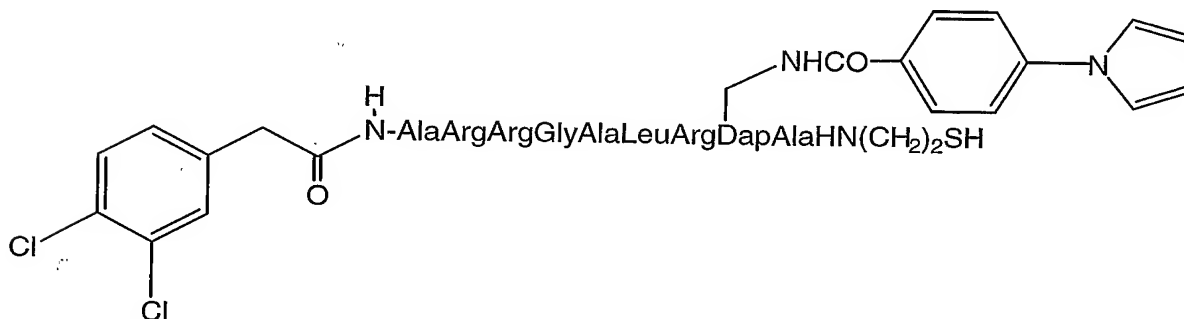


17. The inhibitor of claim 1, comprising



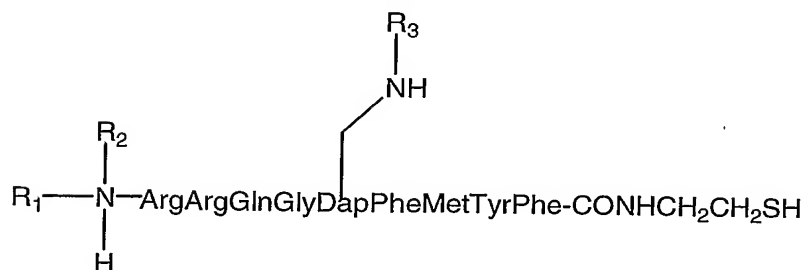
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18. The inhibitor of claim 1, consisting of



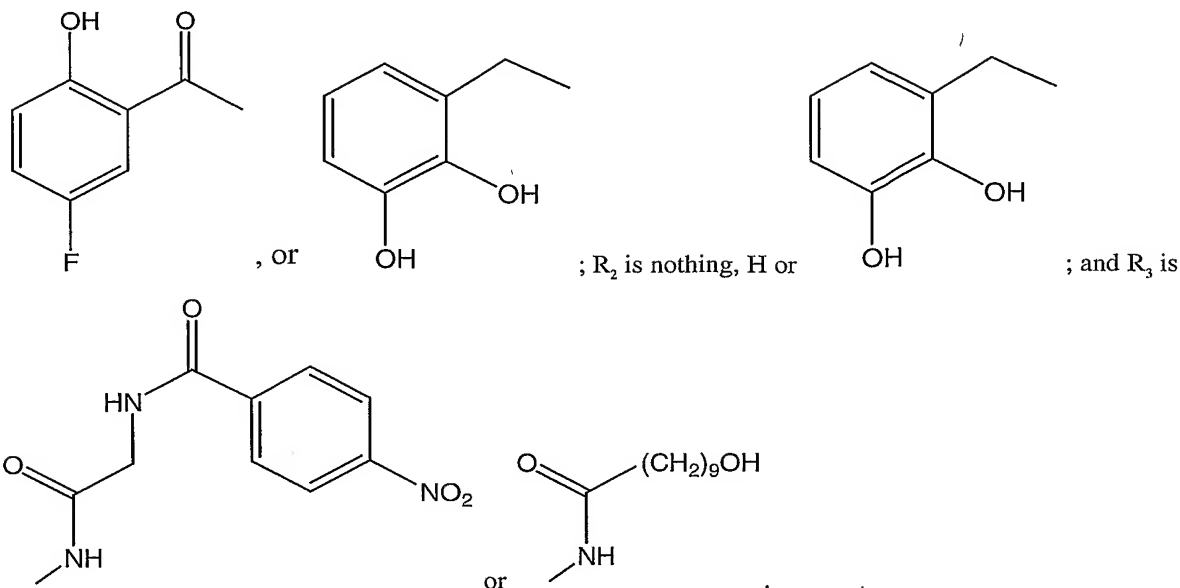
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19. An inhibitor of a protein kinase C (PKC), the inhibitor comprising



wherein R₁ and R₃ are independently H, Ac, a carboxylic acid from FIG. 4, or an aldehyde from FIG. 5, and R₂ is H, a carboxylic acid from FIG. 4, an aldehyde from FIG. 5, or nothing.

20. The inhibitor of claim 19, wherein R_1 is Ac, H,



5

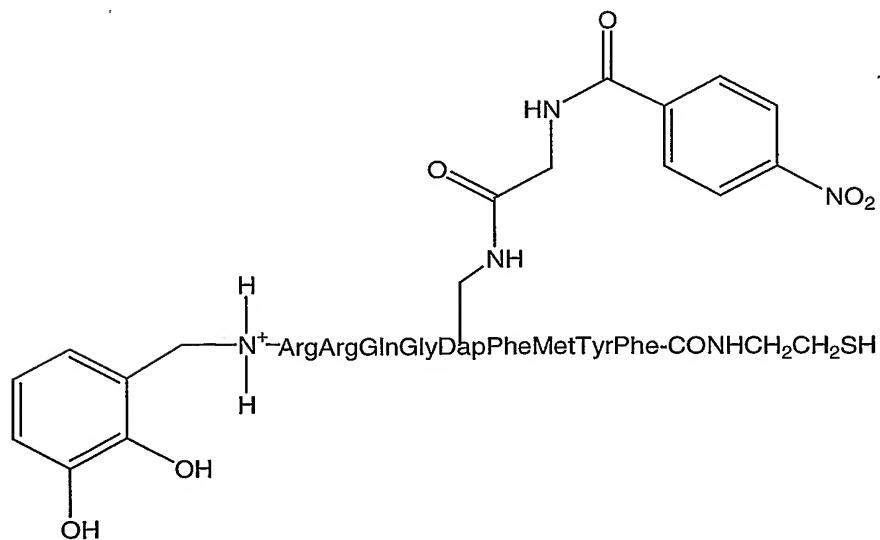
21. The inhibitor of claim 19, comprising Compound B, Compound C, Compound D, Compound E, Compound F, or Compound G of FIG. 7.

22. The inhibitor of claim 19, wherein the inhibitor is specific for a $PKC\beta I$, a $PKC\delta$, and/or a $PKC\zeta$.

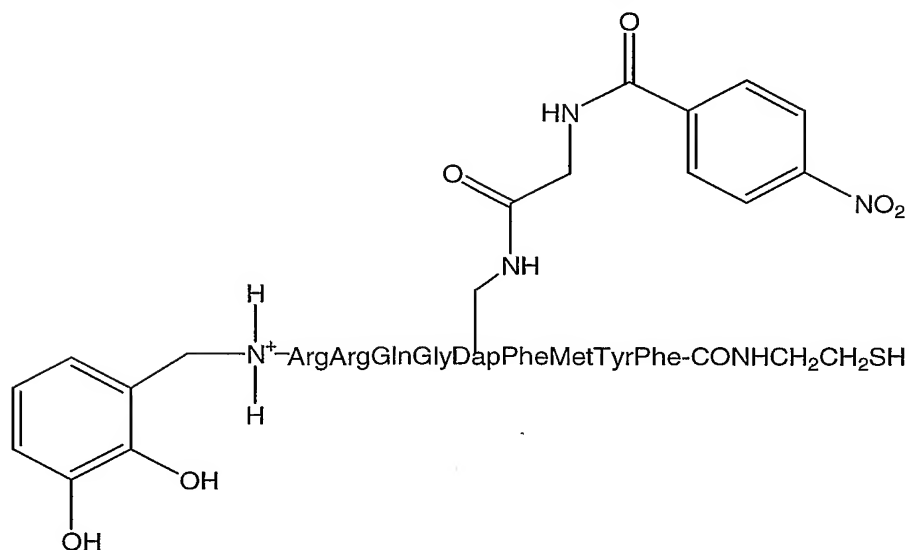
10

23. The inhibitor of claim 19, wherein the inhibitor is specific for a $PKC\delta$.

24. The inhibitor of claim 23, comprising

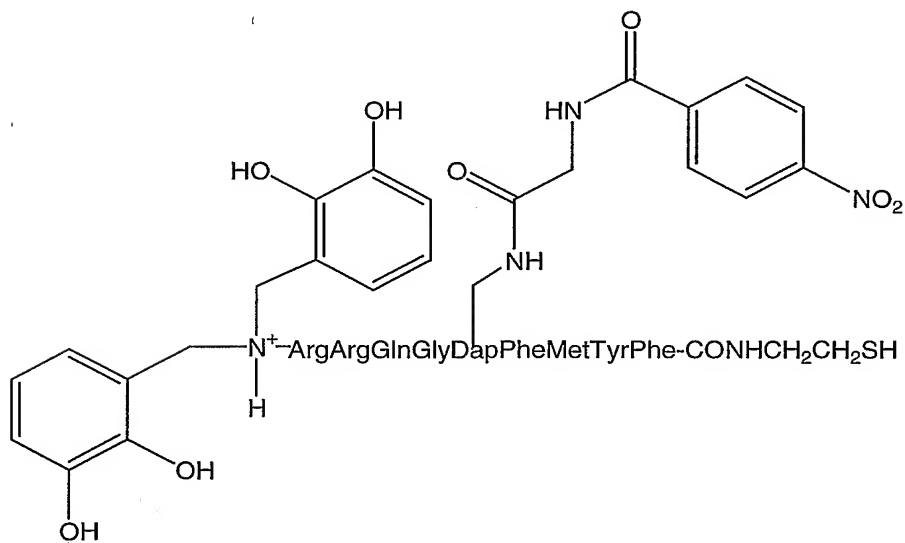


25. The inhibitor of claim 24, the inhibitor consisting of

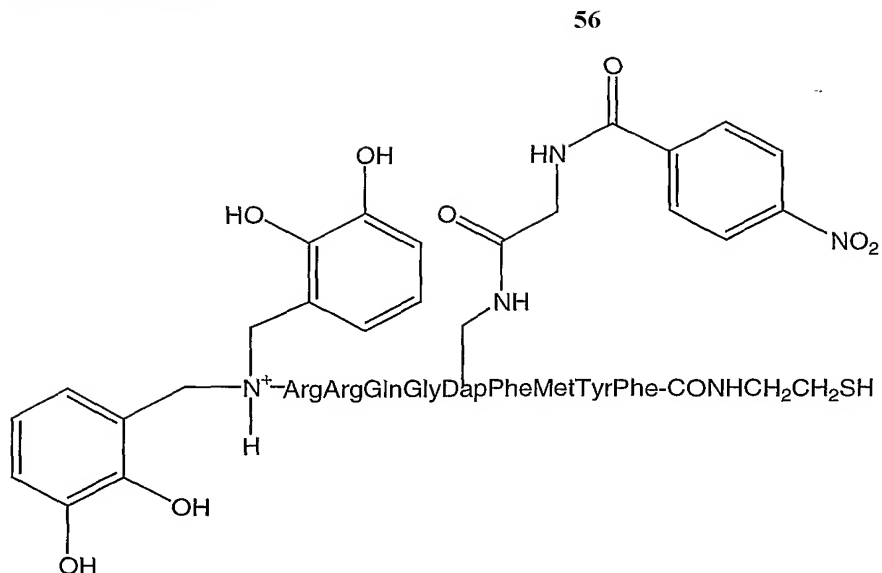


26. The inhibitor of claim 19, wherein the inhibitor is highly selective for a PKC ζ .

27. The inhibitor of claim 26, comprising



28. The inhibitor of claim 26, consisting of



29. A composition comprising the inhibitor of any one of claims 1-28 in a pharmaceutically acceptable excipient.

30. A combinatorial library useful for identifying an inhibitor of a protein kinase, the combinatorial library comprising a plurality of compounds, each compound comprising a consensus sequence for a substrate of the protein kinase, the consensus sequence comprising at least five amino acids or mimetics, wherein at least one amino acid or mimetic is not essential to substrate binding, and wherein an amino acid or mimetic not subject to phosphorylation substitutes a canonical Ser or Thr target residue in the consensus sequence; and a chemical moiety covalently bound to the compound at the at least one non-essential amino acid or mimetic in the consensus sequence and/or the amino acid or mimetic not subject to phosphorylation substituting the canonical Ser or Thr target residue; wherein each compound comprises a different chemical moiety.

31. The combinatorial library of claim 30, wherein the non-essential amino acid or mimetic and/or the amino acid or mimetic substituting a canonical Ser or Thr target residue is a diaminopropionic acid (Dap).

32. The combinatorial library of claim 30, wherein the chemical moiety on each compound is a carboxylic acid.

33. The combinatorial library of claim 32, wherein the carboxylic acid on each compound is selected from any one of the carboxylic acid moieties provided in FIG. 4.

34. The combinatorial library of claim 30, wherein the chemical moiety on each
5 compound is an aldehyde.

35. The combinatorial library of claim 34, wherein the aldehyde is selected from any one of the aldehyde moieties provided in FIG. 5.

10 36. The combinatorial library of claim 30, wherein the chemical moiety is covalently bound to a diaminopropionic acid (Dap).

37. The combinatorial library of claim 30, wherein the chemical moiety is covalently bound to the residue not subject to phosphorylation substituting the canonical Ser or Thr target
15 residue.

38. The combinatorial library of claim 30, wherein the substitute residue is Ala.

39. The combinatorial library of claim 30, wherein the protein kinase is a mammalian
20 protein kinase.

40. The combinatorial library of claim 30, wherein the protein kinase is a human protein kinase.

25 41. The combinatorial library of claim 30, wherein the protein kinase is a protein kinase C (PKC).

42. The combinatorial library of claim 41, wherein the PKC is a PKC α .

30 43. The combinatorial library of claim 42, wherein the consensus sequence for a substrate of the PKC α comprises LysGlySerHyd(Arg/Lys), where Hyd is Phe, Leu or Ile. _

44. The combinatorial library of claim 38, wherein the protein kinase is a PKC α and the consensus sequence with the substituted Ala residue is AlaArgArgGlyAlaLeuArgGlnAla.

35

45. The combinatorial library of claim 30, wherein the protein kinase is a PKC β I and the consensus sequence comprises ArgLysGlySerPheLys.

46. The combinatorial library of claim 30, wherein the protein kinase is a PKC β II and
5 the consensus sequence comprises ArgLysGlySerPheLys.

47. The combinatorial library of claim 30, wherein the protein kinase is a PKC γ and the consensus sequence comprises ArgLysGlySerPheLys.

10 48. The combinatorial library of claim 30, wherein the protein kinase is a PKC δ and the consensus sequence comprises (Lys/Gln)GlySerPhe(Phe/Met).

49. The combinatorial library of claim 30, wherein the protein kinase is a PKC ϵ and the consensus sequence is Lys(Met/Lys)Ser(Phe/Ala)(Glu/Tyr/Asp/Phe).
15

50. The combinatorial library of claim 30, wherein the protein kinase is a PKC η and the consensus sequence is ArgArgSerPheArgArg.

51. The combinatorial library of claim 30, wherein the protein kinase is a PKC ζ and the
20 consensus sequence is (Arg/Gln/Lys/Glu)(Met/Gly)Ser(Phe/Met)(Phe/Met).

52. The combinatorial library of claim 30, wherein the protein kinase is a PKC μ and the consensus sequence is (Gln/Lys/Glu/Met)MetSer(Val/Met/Leu)(Ala/Met/Val).

25 53. The combinatorial library of claim 30, comprising at least 10 compounds.

54. The combinatorial library of claim 30, comprising at least 100 compounds.

55. A method of identifying an inhibitor of a protein kinase, the method comprising
30 creating the combinatorial library of claim 30 for the protein kinase,
screening the compounds in the combinatorial library for inhibitory activity of the
protein kinase, and
identifying any compounds in the combinatorial library that are inhibitors of the protein
kinase.
35

56. The method of claim 55, further comprising creating another combinatorial library from an inhibitor identified in the identifying step.

57. The method of claim 55, wherein each compound is screened separately for
5 inhibitory activity.

58. The method of claim 55, wherein more than one compound is screened together for inhibitory activity.

10 59. The method of claim 55, wherein the protein kinase is a mammalian protein kinase.

60. The method of claim 55, wherein the protein kinase is a human protein kinase.

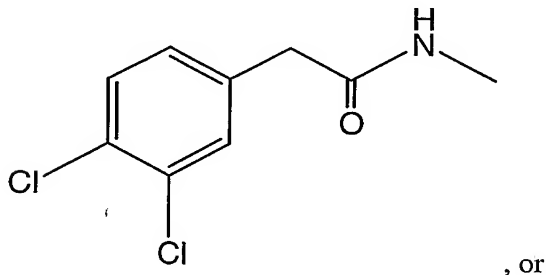
61. The method of claim 55, wherein the protein kinase is a protein kinase C (PKC).
15

62. The method of claim 61, wherein the PKC is a PKC α , a PKC δ , or a PKC ζ .

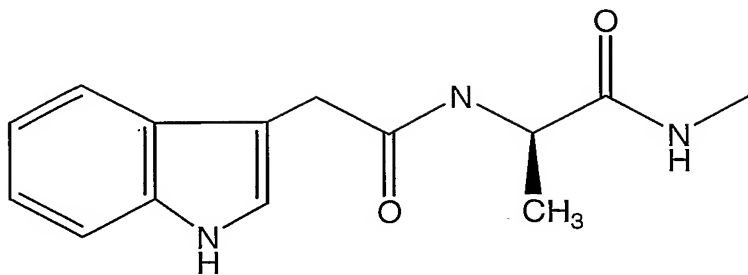
63. A method of treating a deleterious condition in a mammal, where the condition is dependent on a protein kinase C (PKC) for induction or severity, the method comprising
20 contacting the mammal with the composition of claim 29.

64. The method of claim 63, wherein the PKC is a PKC α .

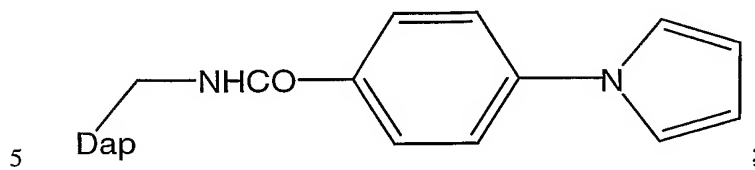
65. The method of claim 64, wherein the inhibitor comprises
25 A-Ala-Arg-Arg-X-B-Hyd-C-D-, where A- =AcHN-,



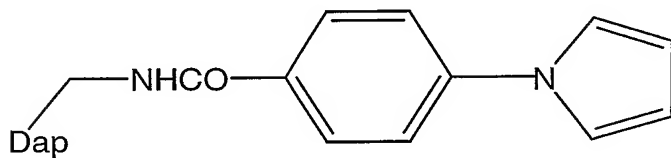
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X=any amino acid or amino acid mimetic; B=Ala or a diaminopropionic acid (Dap) derivative having the formula

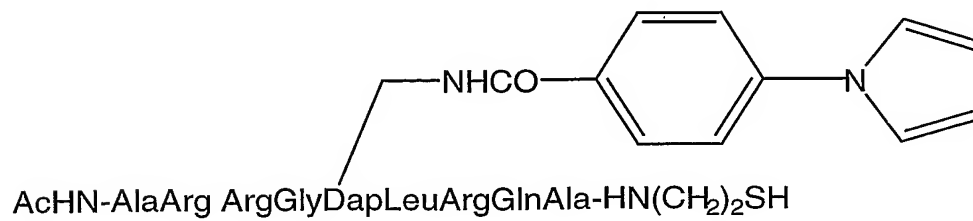
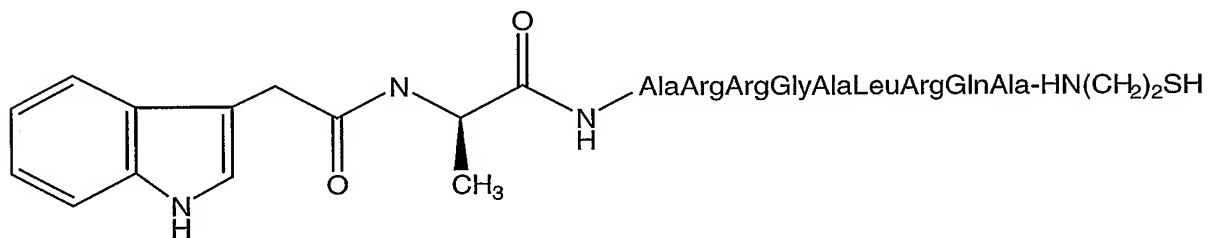


Hyd=Phe, Leu or Ile; C=Arg or Lys; and D=Ala or a Dap derivative having the formula

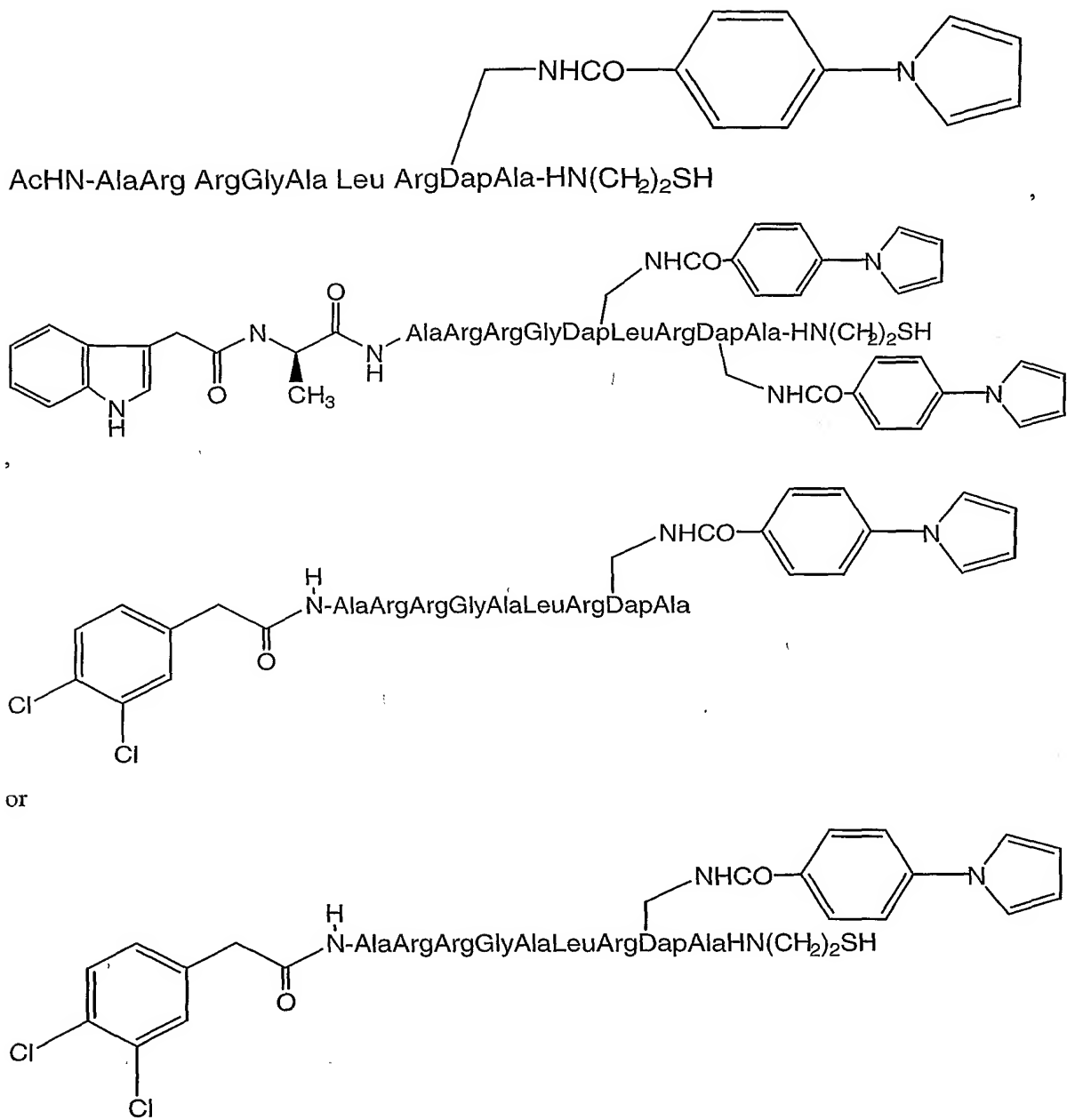


wherein any of the amino acids can alternatively be an analogous amino acid mimetic.

66. The method of claim 64, wherein the inhibitor is

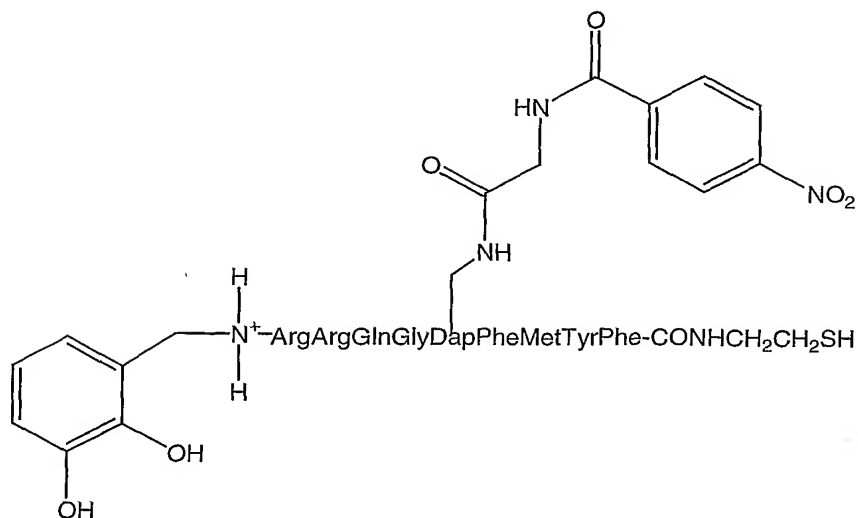


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67. The method of claim 63, wherein the PKC is a PKC δ .

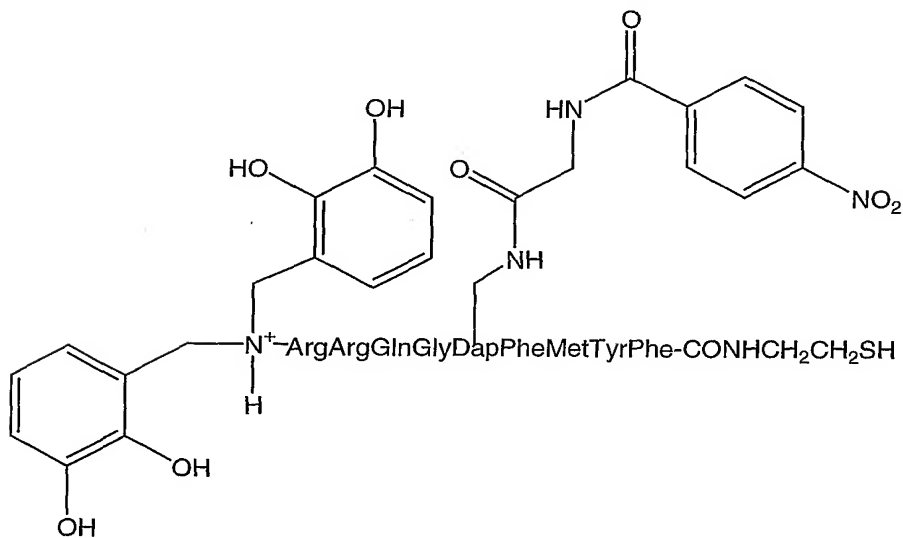
68. The method of claim 67, wherein the inhibitor is



69. The method of claim 63, wherein the PKC is a PKC ζ .

5

70. The method of claim 69, wherein the inhibitor is



10

71. The method of claim 63, wherein the deleterious condition is selected from the group consisting of a cancer, a cardiovascular disease, type 2 diabetes, agammaglobulinaemia, reperfusion injury, Alzheimer's disease, a neurological or neurodegenerative disease, chemotherapy-induced alopecia, arthritis, an autoimmune disease, an inflammatory disease, allergies, asthma and viral virulence.

72. The method of claim 63, wherein the deleterious condition is cancer.

15

73. The method of claim 63, wherein the deleterious condition is heart disease.

74. The method of claim 63, wherein the deleterious condition is type 2 diabetes and the protein kinase is a PKC δ .

5 75. The method of claim 63, wherein the mammal is a human.

76. A method of inhibiting a protein kinase, the method comprising contacting the protein kinase with an inhibitor of the protein kinase C (PKC) of any one of claims 1-28.

10 77. The method of claim 76, wherein the PKC is a mammalian PKC.

78. The method of claim 76, wherein the PKC is in a living mammalian cell.

79. The method of claim 78, wherein the cell is in a living mammal.

15

80. The method of claim 79, wherein the living mammal is a human.

81. The method of claim 79, wherein the mammal has deleterious condition that is dependent on the PKC for induction or severity.

20

82. The method of claim 81, wherein the deleterious condition is selected from the group consisting of a cancer, a cardiovascular disease, type 2 diabetes, agammaglobulinaemia, reperfusion injury, Alzheimer's disease, a neurological or neurodegenerative disease, chemotherapy-induced alopecia, arthritis, an autoimmune disease, an inflammatory disease, 25 allergies, asthma and viral virulence.

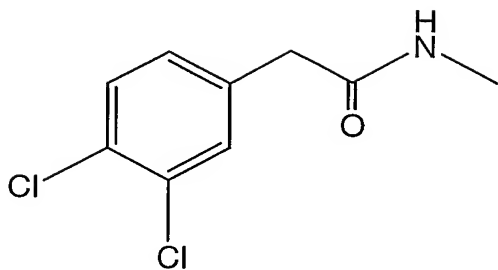
83. The method of claim 81, wherein the deleterious condition is a cancer.

84. The method of claim 76, wherein the PKC is a PKC α .

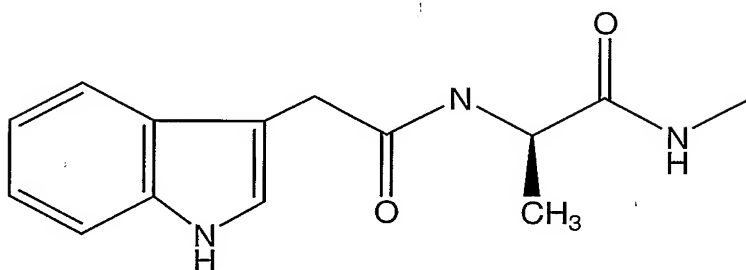
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85. The method of claim 84, wherein the inhibitor comprises A-Ala-Arg-Arg-X-B-Hyd-C-D-, where A- =AcHN-,

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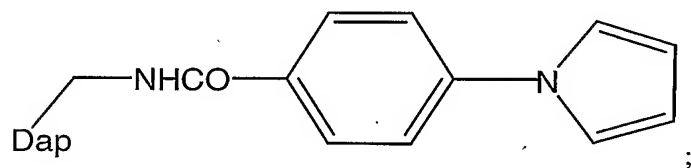


, or



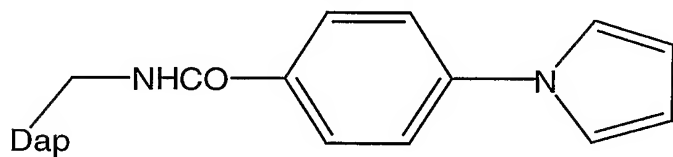
;

- 5 X=any amino acid or amino acid mimetic; B=Ala or a diaminopropionic acid (Dap) derivative having the formula



;

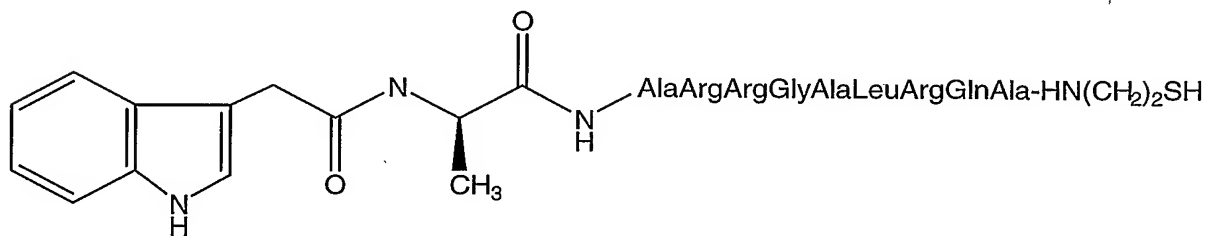
Hyd=Phe, Leu or Ile; C=Arg or Lys; and D=Ala or a Dap derivative having the formula



,

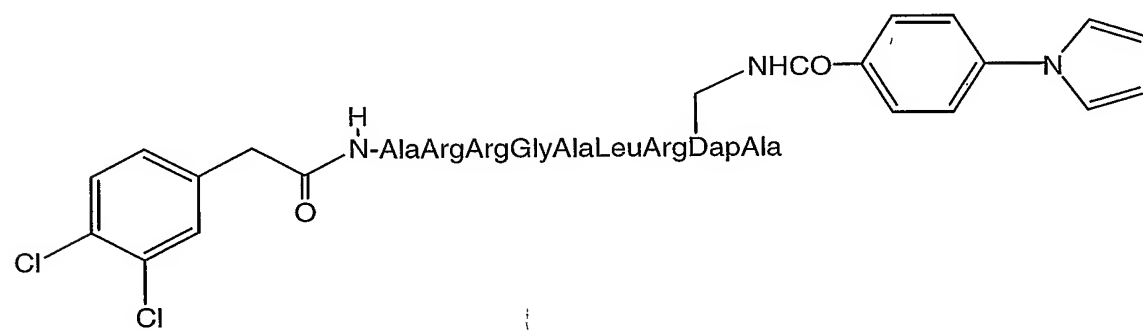
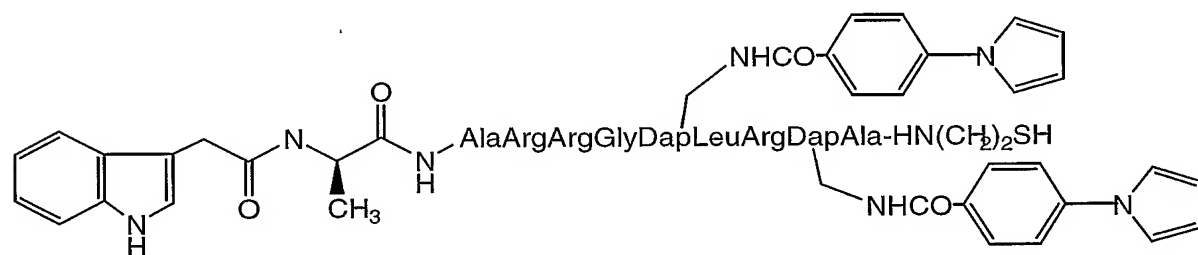
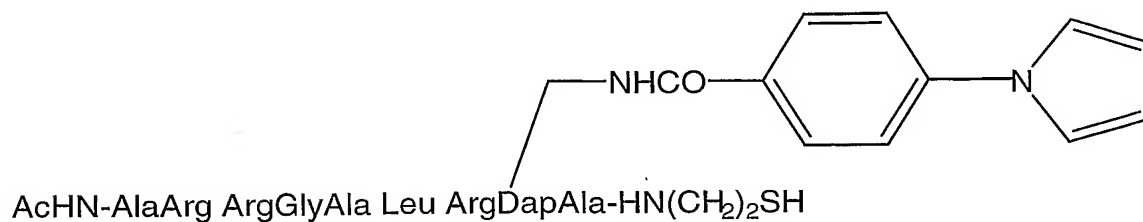
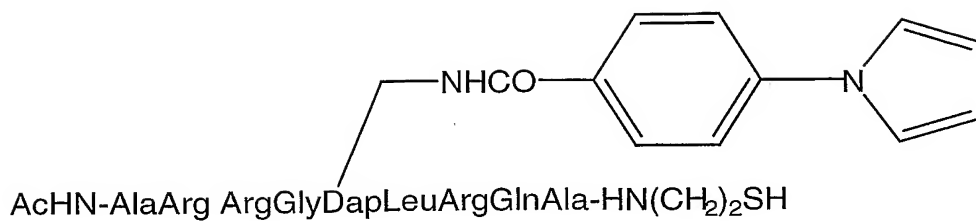
- 10 wherein any of the amino acids can alternatively be an analogous amino acid mimetic.

86. The method of claim 84, wherein the inhibitor is selected from the group consisting of

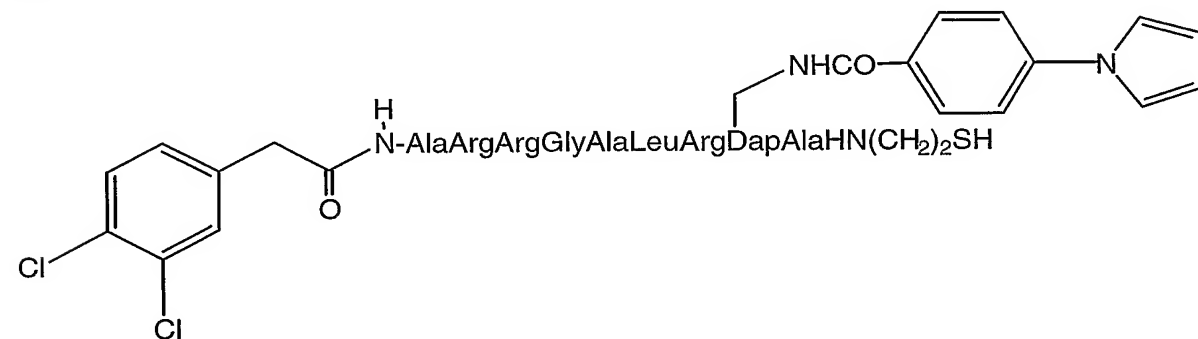


15 ,

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and

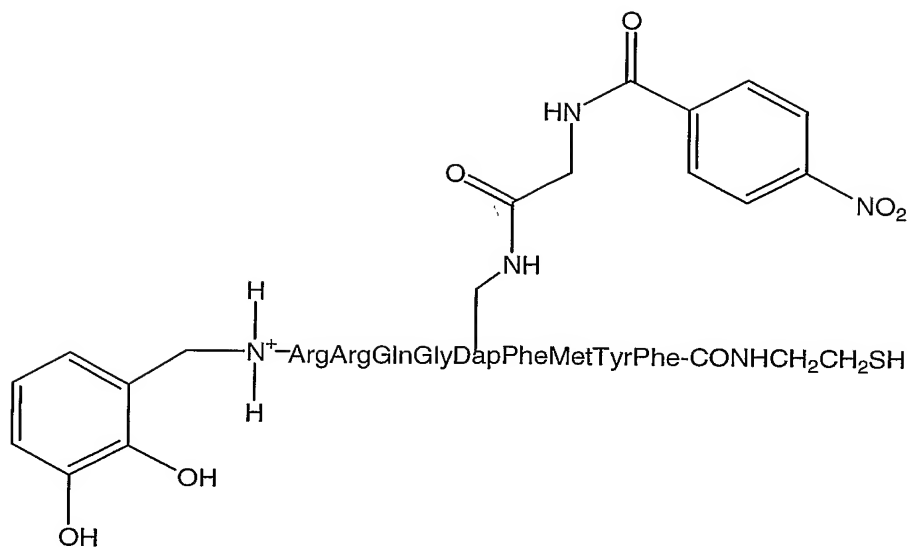


87. The method of claim 76, wherein the PKC is a PKC δ .

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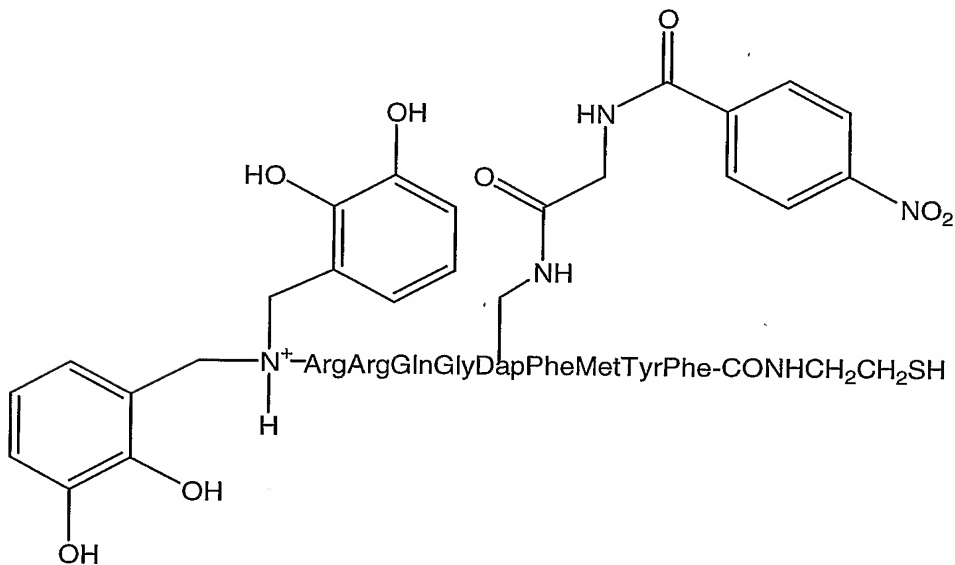
88. The method of claim 87, wherein the inhibitor is

66



89. The method of claim 76, wherein the PKC is a PKC ζ .

90. The method of claim 89, wherein the inhibitor is



91. Use of an inhibitor of a protein kinase in the manufacture of a medicament for the treatment of a deleterious condition in a mammal that is dependent on a protein kinase for induction or severity, the treatment comprising contacting the mammal with an inhibitor of any one of claims 1-28.